UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/568,497	02/16/2006	Martin Ebner	BJS-4145-34	1204

23117 7590 04/15/2009

NIXON & VANDERHYE, PC
901 NORTH GLEBE ROAD, 11TH FLOOR
ARLINGTON, VA 22203

EXAMINER	
SAKELARIS, SALLY A	

ART UNIT	PAPER NUMBER
1797	

MAIL DATE	DELIVERY MODE
04/15/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/568,497	EBNER, MARTIN	
	Examiner	Art Unit	
	Sally A. Sakelaris	1797	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 June 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *14-25* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *14-25* is/are rejected.

7)☒ Claim(s) *20* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *2/16/2006*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Information Disclosure Statement

The information disclosure statement filed 2/16/2006 fails to comply with 37 CFR 1.98(a)(2), which requires a legible copy of each cited foreign patent document; each non-patent literature publication or that portion which caused it to be listed; and all other information or that portion which caused it to be listed. It has been placed in the application file, but the information referred to therein has not been considered.

Claim Objections

Claim 20 is objected to as it appears to include an extra "the" in its first line. Appropriate correction is suggested.

Claim Rejections - 35 USC § 112

Claim 20 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A broad range or limitation together with a narrow range or limitation that falls within the broad range or limitation (in the same claim) is considered indefinite, since the resulting claim does not clearly set forth the metes and bounds of the patent protection desired. See MPEP § 2173.05(c). Note the explanation given by the Board of Patent Appeals and Interferences in *Ex parte Wu*, 10 USPQ2d 2031, 2033 (Bd. Pat.

App. & Inter. 1989), as to where broad language is followed by "such as" and then narrow language. The Board stated that this can render a claim indefinite by raising a question or doubt as to whether the feature introduced by such language is (a) merely exemplary of the remainder of the claim, and therefore not required, or (b) a required feature of the claims. Note also, for example, the decisions of *Ex parte Steigewald*, 131 USPQ 74 (Bd. App. 1961); *Ex parte Hall*, 83 USPQ 38 (Bd. App. 1948); and *Ex parte Hasche*, 86 USPQ 481 (Bd. App. 1949). In the present instance, claim 20 recites the broad recitation "the polar solvent is water, methanol, ethanol or an admixture thereof", and the claim also recites "preferably the mobile phase comprises at least 60% water" which is the narrower statement of the range/limitation.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

1. Claims 14-20 and 22-24 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lacey et al. (Journal of Chromatography, 315 (1984) 233-241) in view of Bartha et al.(Chromatographia Vol. 20, No. 10, October 1985).

With regard to claims 14 -16 and 19, 20, 22 – 24 Lacey et al teach a method for assaying free tropolone derivatives (II and IV, Fig.1) as a part of a method for identifying and quantitating the various decomposition products of colchicine using a reversed-phase(RP) HPLC method which utilizes complexation with the copper (II) ion. Lacey teach the separation of colchine and colchiside in Colchicum seeds consisting of a proteinaceous solution containing an enriched product protein (Pg. 234). Lacey et al next teach that the failure of colchiceine to elute was due to the hydroxytropone moiety, as trimethylcolchicinic acid also failed to elute under these conditions. The reference then teaches that due to these difficulties it was preferable to investigate further separation methods based on the extensive previous studies in this field of the art.

With regard to 15 and 16, Lacey et al teaches that separation was achieved using the hydrophobic stationary phase of a reversed-phase C_{18} radial compression, silica packed cartridge. (Pg. 235).

With regard to claims 19 and 20, Lacey et al teach that the organic phase was a mixture of methanol-acetonitrile (25:75) and that all data obtained used a 35% organic phase.

With regard to claims 22-24, Lacey et al teach that the compounds were eluted using miscible, acetonitrile-methanol-1% copper sulphate solution at pH 4.0 (26.25:8,75:65) in the caption of Figure 7 and in the top right corner of page 239. Lacey

also teaches that decreasing the percentage of $CuSO_4$ from 1.50 to 0.25% resulted in an increase in both retention time and peak width of II and IV (Fig.6).

With regard to claim 14, Lacey et al. does not teach the assay for tropolone that uses both Cu(II) ions and an ion-pairing reagent that is further characterized in that it is more hydrophobic than trifluoroacetic acid (TFA).

With regard to claims 17 and 18, Lacey et al. does not teach the ion pairing reagent having a dielectric constant equal to hexylsuphonic acid.

However, with regard to claims 14, 17, and 18 Bartha et al. teach the effect of the type of ion-pairing reagent in reversed-phase ion-pair chromatography and teach the inclusion of an ion pairing reagent more hydrophobic than TFA (Summary). Bartha et al. teach that the effects of the type of pairing ion were examined by comparing solute retention changes as a function of both mobile and stationary phase concentrations of the various sulfonic acid pairing ions. Specifically, Bartha et al teaches the behavior of various alkylsulfonic acids of varying chain length including hexylsulphonic acid.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to have included an ion-pairing reagent such as hexylsuphonic acid into the assay for tropolone as it is known that ion pairing can improve the solute retention of the method and can decrease the peak tailing present in RP HPLC data. Furthermore, Bartha et al. provides that alkylsulfonic acids of varying chain length "are interchangeable at indentical surface concentrations in influencing retention" (pg. 590).

2. Claims 21 and 25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lacey et al. (Journal of Chromatography, 315 (1984) 233-241) in view of Bartha et al.(Chromatographia Vol. 20, No. 10, October 1985) and in further view of Zabrecky et al (US Patent 5,179,199).

The teachings of Lacey in view of Bartha can be seen above.

With regard to claim 21, Lacey et al. in view of Bartha does not teach that the precipitation of tropolone with $CuSO_4$ precedes removing protein from the recovered precipitate by ultrafiltration.

With regard to claim 25, Lacey in view of Bartha does not teach the method wherein the supernatant comprising the protein is enriched to a concentration of 1 mg/ml or higher.

With regard to claim 21, Zabrecky et al. teaches a method of removing an organic solvent from a mixture that includes a compound having a polypeptide and an organic solvent, the method including the steps of contacting the mixture with an ion exchange resin under conditions that allow the compound to bond to the resin; and washing the resin with a first aqueous solution that elutes the organic solvent from the resin while allowing the protein to remain bound to the resin. Finally, the protein may be eluted from the resin. (claims 5, 6, and 7).

With regard to claim 25, Zabrecky teaches an ion exchange chromatography and RP HPLC methods in their examples 1-3 wherein EPO's (their protein of interest) recovery was greater than 90% and at a purity of 99% (Col. 3 and 4).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the columns of Zabrecky to have firstly precipitated tropolone with $CuSO_4$ as this method was showed by Lacey et al. to bind tropolone with very high affinity and to have secondly to have recovered the protein following ultrafiltration as taught by Zabrecky as it is important to provide bio-products as pure as possible in order to prevent deterioration but also to avoid averse toxic reactions when products are administered. Also, Zabrecky et al. teach that their method of protein purification provides a simple, inexpensive, and rapid method of removing organic solvents from a protein solution (Col. 2 lines 4-7).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sally A. Sakelaris whose telephone number is 5712726297. The examiner can normally be reached on Monday-Friday 8-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jill Warden can be reached on 5712721267. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Sally Sakelaris

/Jill Warden/
Supervisory Patent Examiner, Art Unit 1797